

Tumor Ablation with Irreversible Electroporation

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We report the first successful use of irreversible electroporation for the minimally invasive treatment of aggressive cutaneous tumors implanted in mice. Irreversible electroporation is a newly developed non-thermal tissue ablation technique in which certain short duration electrical fields are used to permanently permeabilize the cell membrane, presumably through the formation of nanoscale defects in the cell membrane. Mathematical models of the electrical and thermal fields that develop during the application of the pulses were used to design an efficient treatment protocol with minimal heating of the tissue. Tumor regression was confirmed by histological studies which also revealed that it occurred as a direct result of irreversible cell membrane permeabilization. Parametric studies show that the successful outcome of the procedure is related to the applied electric field strength, the total pulse duration as well as the temporal mode of delivery of the pulses. Our best results were obtained using plate electrodes to deliver across the tumor 80 pulses of 100 μ s at 0.3 Hz with an electrical field magnitude of 2500 V/cm. These conditions induced complete regression in 12 out of 13 treated tumors, (92%), in the absence of tissue heating. Irreversible electroporation is thus a new effective modality for non-thermal tumor ablation.

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INTRODUCTION

Minimally invasive tissue ablation has become of central importance in the modern surgery armamentarium. In the treatment of benign or malignant tumors it is important to achieve ablation of the undesirable tissue in a well-controlled and precise way without affecting the surrounding healthy tissue. As an alternative to surgical resection, a number of minimally invasive methods have been developed to destroy specific areas of undesirable tissues. Most of these techniques are thermal using cold, e.g. cryosurgery [1–3] or heat, e.g. radiofrequency [4,5].

Electroporation, also known as electroporation, is a term used to describe the permeabilization of the cell membrane as a consequence of the application of certain short and intense electric fields across the cell membrane, the cells or the tissues. The permeabilization can be temporary (reversible electroporation) or permanent (irreversible electroporation) as a function of the electrical field magnitude and duration, and the number of pulses [6]. Reversible electroporation is commonly used *in vivo* to facilitate the penetration of various otherwise non-permeable macromolecules across the cell membrane [7–9]. Irreversible electroporation, the ability of certain electrical pulses to permanently permeabilize the cell membrane, has been known for over three decades. For most of this period irreversible electroporation (IRE) was used primarily for ablation of microorganisms and cells *in vitro* and studied only as an upper limit of electrical parameters for reversible tissue electroporation applications. Our group has pursued the understanding of the electrical fields and processes that produce IRE with single cell micro-electroporation technology [10,11].

The study of Davalos, Mir and Rubinsky, which showed that IRE can ablate substantial volumes of tissue without inducing a thermal effect and therefore serve as an independent and new tissue ablation modality, opened the way to the use of IRE in surgery [12]. Subsequently, Eddi *et al.* demonstrated tissue ablation with IRE *in vivo* in the normal liver of rats. [13]. Complete ablation of the targeted liver tissue was achieved by exposing the tissue to

electrical parameters that do not induce thermal damage [13]. Massive blood vessel congestion was observed in the sinusoids of the treated volume, which should significantly enhance the treatment. The study concluded that IRE produces precisely delineated ablation zones with cell scale resolution between ablated and non-ablated areas and the ability of mathematical modelling to precisely predict the ablated area. A more recent study was performed to evaluate the long term effects of IRE in a large animal model [14]. The results demonstrated the ability of electroporation to ablate large volumes of tissue using electrical parameters that while substantially above those conventionally used in reversible electroporation do not induce substantial thermal effects. The histology has reconfirmed the results in Davalos *et al.* [12] and Eddi *et al.* [13] showing that mathematical modeling of electrical and thermal fields are a powerful tool in designing IRE ablation protocols, that IRE can be used to ablate tissue with cell scale resolution and that indeed IRE affects only the cell membrane and therefore spares connective tissue. Another

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Competing Interests: R. Davalos and B. Rubinsky have potential interests in the revenues of pending patents held by Univ. of California at Berkeley (e.g. No 10/371,162, Tissue Ablation with Irreversible Electroporation). B. Rubinsky also has a financial interest in Excellen Life Sciences and in Oncobionics, companies in the field of electroporation. L. M. Mir was a consultant for Oncobionics.

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Jian Zhou



New Technologies Tumor Ablation Irreversible Electroporationchinese Edition:

Emerging technologies and biology for tumor microenvironment and tumor-immune interplay Min Xue,Qihui Shi,Li Cao,2022-12-08 **Tumor Ablation and Immunity** Yueyong Xiao,Ming Kuang,Nikolai Korpan,2024-02-29 *Recent Advances in the Understanding of Hepatocellular Carcinogenesis, 2nd edition* Prasanna K. Santhekadur,Bubu Ama Banini ,Rohini Mehta,2024-09-19 Hepatocellular carcinoma HCC is the most common cancer of the liver and the third most cause of cancer related deaths worldwide The 5 year survival of HCC is less than 20% making HCC the second most lethal malignancy the first being pancreatic cancer HCC usually occurs in patients with chronic liver disease in association with a variety of risk factors including chronic liver infection with hepatitis B virus or hepatitis C virus excessive consumption of alcohol overeating obesity and nonalcoholic fatty liver disease other metabolic liver diseases including Wilson s disease hemochromatosis and alpha 1 antitrypsin deficiency and environmental toxins such as aflatoxins Tobacco use and human immunodeficiency virus infection also increases the risk of HCC The heterogeneity of HCC associated with different etiologies affects tumor initiation development and progression thus limiting the identification of consistent or routinely occurring genetic abnormalities characteristic of this malignancy Nevertheless sustained inflammation hepatocyte regeneration and apoptosis occurring in chronic liver disease results in fibrosis and ultimately cirrhosis favoring genetic and epigenetic modifications that lead to the formation of dysplastic nodules and eventually oncogenesis Identification of novel diagnostic and prognostic biomarkers for HCC is an unmet need in this current era The aim of this Research Topic is to provide insights on novel aspects of HCC diagnosis prognostication and therapy with an emphasis on recent and up to date findings from the scientific literature Genetic and molecular signatures arising from HCC in association with specific etiologies and implications for cancer screening and surveillance will be discussed As indicated sub topics listed below Original articles Reviews and Mini Review articles will address all areas of HCC relevant not only to basic and clinical researchers but also to practitioners in various fields of medicine 1 Epidemiology of Hepatocellular carcinoma 2 Risk factors for hepatocellular carcinoma 3 Nonalcoholic Fatty Liver Disease and Hepatocellular Carcinoma 4 Animal models for studying hepatocellular carcinoma 5 Hepatocellular Carcinoma Oncogenes 6 Tumor suppressors and Novel regulators of Hepatocellular Carcinoma 7 MicroRNA and Hepatocellular Carcinoma 8 Circulating biomarkers of Hepatocellular Carcinoma

Irreversible Electroporation in Clinical Practice Martijn R. Meijerink,Hester J. Scheffer,Govindarajan Narayanan,2017-12-27 This book provides a comprehensive overview of the clinical use of irreversible electroporation IRE better known by its commercial name NanoKnife which is one of the most exciting new needle guided cancer treatments The coverage includes the history of IRE general technique preclinical research applications in clinical practice and early clinical results and future perspectives Contraindications treatment planning potential complications follow up imaging and other practical aspects are fully discussed with highlighting of useful tips and tricks Through the delivery of short but highly

intense electrical pulses IRE results in tumor cell membrane permeabilization causing cells to go into apoptosis The minimally invasive nature of IRE combined with the prospect of completely eradicating tumors while preserving delicate structures in the ablation zone makes IRE the object of worldwide clinical research This book will be of value for practitioners and trainees in interventional and diagnostic radiology surgery medical oncology HPB and gastroenterology urology and radiation oncology The Proceedings of the 17th Annual Conference of China Electrotechnical Society Kaigui Xie,Jianlin Hu,Qingxin Yang,Jian Li,2023-03-30 This book gathers outstanding papers presented at the 17th Annual Conference of China Electrotechnical Society organized by China Electrotechnical Society CES held in Beijing China from September 17 to 18 2022 It covers topics such as electrical technology power systems electromagnetic emission technology and electrical equipment It introduces the innovative solutions that combine ideas from multiple disciplines The book is very much helpful and useful for the researchers engineers practitioners research students and interested readers **Advances in imaging and imaging-directed interventions in hepatic cancers** Xiankai Sun,Chandan Guha,2023-08-30

Irreversible Electroporation Boris Rubinsky,2009-11-25 Non thermal irreversible electroporation is a new minimally invasive surgical procedure with unique molecular selectivity attributes in fact it may be considered the first clinical molecular surgery procedure Non thermal irreversible electro ration is a molecular selective mode of cell ablation that employs brief electrical fields to produce nanoscale defects in the cell membrane which can lead to cell death without an effect on any of the other tissue molecules The electrical fields can be produced through contact by insertion of electrode needles around the undesirable tissue and non invasively by electromagnetic induction This new dition to the medical armamentarium requires the active involvement and is of interest to clinical physicians medical researchers mechanical engineers che cal engineers electrical engineers instrumentation designers medical companies and many other fields and disciplines that were never exposed in their training to irreversible electroporation or to a similar concept This edited book is designed to be a comprehensive introduction to the field of irreversible electroporation to those that were not exposed or trained in the field before and can also serve as a reference manual Irreversible electroporation is broad and interdisciplinary Therefore we have made an attempt to cover every one of the various aspects of the field from an introductory basic level to state of the art

Nanomedicine Yujun Song,2024-07-31 A comprehensive and multidisciplinary guide to nanomaterials based medicine Nanomedicine is the study and application of nanomaterials based medical techniques In recent years it has very rapidly become indispensable in a huge range of medical contexts from analysis of extreme life events to diagnosis and treatment of life threatening intractable diseases such as cancers and cardiovascular diseases It has already transformed both research and clinical outcomes in many areas of medicine and promises to continue as the cutting edge research and clinical area for the next generation of medical specialists Nanomedicine Fundamentals Synthesis and Applications constitutes a comprehensive guide to this subfield and its recent advances Beginning with a brief history of the field and introduction to its

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Diagnosis and Treatment Surgery, 16th Edition Gerard M. Doherty, 2024-12-20 The evidence based point of care information you need to master the full scope of diseases and disorders most often treated by surgeons Organized by organ system Current Diagnosis and Treatment Surgery begins with the relationship between surgeons and their patients training and professionalism preoperative care postoperative care and surgical complications Subsequent chapters cover wound healing inflammation infection antibiotics fluid and electrolyte management and surgical metabolism and nutrition In addition to sections covering everything from head and neck tumors to hand surgery this comprehensive resource offers expert coverage of pediatric surgery oncology weight management organ transplantation and more Featuring 600 photographs and illustrations hundreds of chapter ending multiple choice review questions and the latest the latest research and discoveries Current Diagnosis and Treatment Surgery is designed to help you find all the answers you need quickly and easily 1st World Congress on Electroporation and Pulsed Electric Fields in Biology, Medicine and Food & Environmental Technologies

Tomaz Jarm, Peter Kramar, 2015-08-31 This volume presents the proceedings of the 1st World Congress on Electroporation and Pulsed Electric Fields in Biology Medicine and Food Environmental Technologies WC2015 The congress took place in Portoro Slovenia during the week of September 6th to 10th 2015 The scientific part of the Congress covered different aspects of electroporation and related technologies and included the following main topics Application of pulsed electric fields technology in food challenges and opportunities Electrical impedance measurement for assessment of electroporation yield Electrochemistry and electroporation Electroporation meets electrostimulation Electrotechnologies for food and biomass treatment Food and biotechnology applications In vitro electroporation basic mechanisms Interfacial behaviour of lipid assemblies membranes and cells in electric fields Irreversible electroporation in clinical use Medical applications electrochemotherapy Medical applications gene therapy Non electric field based physical methods inducing cell poration and enhanced molecule transfer Non thermal plasmas for food safety environmental applications and medical treatments PEF for the food industry fundamentals and applications PEF proce ss integration complex process chains and process combinations in the food industry Predictable animal models Pulsed electric fields and electroporation technologies in bioeconomy Veterinary medical applications **Associating Liver Partition and Portal Vein Ligation for Staged**

Hepatectomy (ALPPS) Jian Zhou,2025-07-17 This book systematically describes details in Associating liver partition and portal vein ligation for staged hepatectomy ALPPS The chapters focus on the development history applied anatomy mechanism of action specific methods of administration of the various types of current ALPPS procedures from classical ALPPS to various modified procedures the preoperative evaluation case selection indications and contraindications and surgical planning as well as the postoperative management and follow up treatment It also introduces the progress of international research on ALPPS as well as the ALPPS modeling of the research It will be a helpful reference for hepatobiliary surgeons and oncologists to learn the latest theoretical and technical knowledge about ALPPS The Proceedings of the 17th Annual Conference of China Electrotechnical Society Jian Li,Kaigui Xie,Jianlin Hu,Qingxin Yang,2023-03-31 This book gathers outstanding papers presented at the 17th Annual Conference of China Electrotechnical Society organized by China Electrotechnical Society CES held in Beijing China from September 17 to 18 2022 It covers topics such as electrical technology power systems electromagnetic emission technology and electrical equipment It introduces the innovative solutions that combine ideas from multiple disciplines The book is very much helpful and useful for the researchers engineers practitioners research students and interested readers *Interventional Oncology* Jean-Francois H. Geschwind,Michael C. Soulen,2016-09-22 A comprehensive guide to the full range of interventional oncology techniques and their use in cancer diagnosis and management Advanced Electroporation Techniques in Biology and Medicine Andrei G. Pakhomov,Damijan Miklavcic,Marko S. Markov,2010-06-02 During the last several decades intense study has taken place on the effects of electromagnetic fields on living tissues Reflecting this inquiry this book discusses the theoretical and experimental evidence of these electromagnetic fields and electric pulses and examines their importance in medicine and biology The authors present the basic techniques applied in electroporation and the advanced methods for creation of nanopores highlighting their basic science and clinical applications Topics include nano electroporation classic electroporaiton experimental evidence for electroporation of living cells and electroporation for cancer and wound healing The Proceedings of the 18th Annual Conference of China Electrotechnical Society Qingxin Yang,Zewen Li,An Luo,2024-04-01 This book gathers outstanding papers presented at the 18th Annual Conference of China Electrotechnical Society organized by China Electrotechnical Society CES held in Nanchang China from September 15 to 17 2023 It covers topics such as electrical technology power systems electromagnetic emission technology and electrical equipment It introduces the innovative solutions that combine ideas from multiple disciplines The book is very much helpful and useful for the researchers engineers practitioners research students and interested readers Gastrointestinal Oncology Janusz A. Z. Jankowski,2024-01-15 GASTROINTESTINAL ONCOLOGY Blends quality research findings with advanced educational techniques in a uniquely comprehensive approach Written and edited by leading international experts in the field *Gastrointestinal Oncology A Critical Multidisciplinary Team Approach* is an indispensable reference for clinicians medical

practitioners and trainees involved in the investigation diagnosis and treatment of esophageal gastric intestinal colonic hepatobiliary pancreatic and other gastrointestinal tumors Drawing on the most current evidence based knowledge this comprehensive resource reflects the current care of GI cancer patients enabling effective clinical decision making and patient management Setting the standard in clinical practice Gastrointestinal Oncology remains the only truly multidisciplinary reference designed for the diverse team of clinicians responsible for different stages of cancer treatment Specially structured clinical chapters each representing a different role in the multidisciplinary team MDT allow clear presentation and quick reference of the contents This is supported by a wealth of high quality color photographs line drawings and diagrams Now in its second edition this authoritative reference is fully updated to reflect groundbreaking research in multiple medical fields including the explorative use of A I New sections on palliative care and nutrition are accompanied by new sub sections on molecular characterization new targeted small molecule receptor options and immunological therapies for each cancer This edition places renewed emphasis on the most ubiquitous conditions such as colon cancer liver cancer and gastro esophageal cancer Covering the oncology of the entire gastrointestinal tract Gastrointestinal Oncology A Critical Multidisciplinary Team Approach is a must have reference for the entire MDT including gastroenterologists hepatologists GI surgeons medical oncologists radiation therapists interventional radiologists pathologists nutritionists palliative care and specialist nurses as well as clinical scientists *Interventional Radiology* Bradley B. Pua, Anne M. Covey, David C. Madoff, 2018-11-12 In 2012 the American Board of Medical Specialties ABMS approved Interventional Radiology IR as its own specialty Born out of the field of Diagnostic Radiology IR requires a more clinical focus on initial consultation and post procedural management rather than its previous role of performing image guided procedures Interventional Radiology Fundamentals of Clinical Practice is written with this new focus in mind to help readers incorporate their procedural knowledge into a holistic approach of patient management Chapters explore topics across a broad spectrum of IR with a focus on etiology and pathophysiology of disease followed by discussions on intra procedural and post procedural management Numerous tables and boxes and over 420 total figures complement chapter content This comprehensive text is a must have for IR residents and all practicing interventional radiologists *Enhanced Electric Pulse Technology for the Ablation of Pancreatic Cancer* Siqi Guo, 2018 Electric pulse based technology has been developed and studied as a non thermal ablation method for local control of pancreatic cancer Irreversible electroporation IRE has shown a significant survival benefit for local advanced pancreatic cancer in clinical trials However incomplete ablation with local recurrence and major complications limit the potential of this new technology We have developed an integrated moderate heating electric pulse delivery system which consists of controllable tumor heating multi parameter monitoring and electric pulse delivery The impedance of tumor is greatly decreased after moderate heating at 42 C for 1 2 min which does not cause any cell death Moderate heating significantly enlarges the ablation zone of tumor treated with IRE

In contrast to IRE alone moderate heating assisted IRE results in a high rate of complete tumor regression and a significant longer median survival Another electric pulse technology nanosecond electric pulses has been assessed for the treatment of pancreatic cancer as well Nanosecond electric pulse treatment achieves more survival benefit in animals with partial tumor ablation than those treated with IRE and leads to a vaccine like protective effect in animals with complete local ablation More studies are needed to demonstrate the advantages and translational feasibility of the enhanced electric pulse technologies

Irreversible Electroporation in Clinical Practice Martijn R. Meijerink, Hester J. Scheffer, Govindarajan

Narayanan, 2019-06-04 This book provides a comprehensive overview of the clinical use of irreversible electroporation IRE better known by its commercial name NanoKnife which is one of the most exciting new needle guided cancer treatments The coverage includes the history of IRE general technique preclinical research applications in clinical practice and early clinical results and future perspectives Contraindications treatment planning potential complications follow up imaging and other practical aspects are fully discussed with highlighting of useful tips and tricks Through the delivery of short but highly intense electrical pulses IRE results in tumor cell membrane permeabilization causing cells to go into apoptosis The minimally invasive nature of IRE combined with the prospect of completely eradicating tumors while preserving delicate structures in the ablation zone makes IRE the object of worldwide clinical research This book will be of value for practitioners and trainees in interventional and diagnostic radiology surgery medical oncology HPB and gastroenterology urology and radiation oncology

The Molecular Selectivity of Non-Thermal Irreversible Electroporation and Tissue Regeneration In Vivo Mary Alice Phillips, 2012 Non thermal irreversible electroporation NTIRE is new minimally invasive surgical technique for tissue ablation that utilizes molecular selectivity to ablate tissue tumors Short microsecond electrical pulses are applied to the tissue selectively targeting the cell membrane causing pores to form within the membrane and leading to cell death This tissue ablation technique has potential for a variety of medical applications and has shown great promise as a method for treating cancer tumors NTIRE has many promising attributes as a treatment modality such as the preservation of tissue scaffolding and the blood vessels Very little work however has been done in examining how the molecular selectivity of NTIRE affects tissue regeneration This work examines how tissues regenerate and recover after NTIRE with a focus on those critical tissues that are particularly susceptible to collateral damage from treating an adjacent tumor Two important tissues are examined the artery and the small intestine The artery may be embedded within a tumor Although complete tumor ablation is desired it is important that the artery can recover quickly in order to aid in overall tissue regeneration at the treated site It is also important to understand how the molecular selectivity of NTIRE affects the regeneration of the small intestine especially for the application of abdominal cancer treatment Damage to the small intestine is often the limiting factor in other types of cancer treatments such as localized radiation therapy causing pain and discomfort and even resulting in stopping the treatment early Understanding how the small intestine recovers after NTIRE is

essential in developing this technology for treating abdominal cancers such as pancreatic cancer. Finite element models were utilized to design electrical parameters for both the artery and the small intestine that would cause irreversible electroporation to occur within the tissue while avoiding thermal damage due to Joule heating effects. These electrical parameters were then applied in vivo. Electrical parameters chosen to apply to the artery were an electric field of 1750 V/cm, 90 pulses of a pulse length of 100 μ s and a frequency of either 1 or 4 Hz. The chosen small intestine electroporation protocol consisted of 2000 V/cm, 50 pulses of 70 μ s each and a frequency of 4 Hz. Additional finite element analysis was used to examine the effect of the heterogeneity of tissues such as the small intestine, indicating that changes in electrical conductivity from layer to layer is an important factor that should be accounted for in clinical treatment planning and future work should include quantifying these electrical conductivity values. By applying NTIRE to the rat carotid artery, the recovery of the artery over the week following treatment was observed. It was demonstrated that the electroporation protocol preserved the native tissue extracellular matrix. Three days after NTIRE treatment, the ablated cells had been naturally removed from the tissue, leaving a decellularized construct. By one week after electroporation, new endothelial cells were seen lining the artery lumen. This endothelial layer indicates that normal recellularization is taking place and that the artery is beginning to recover within 7 days of treatment. In a similar fashion, NTIRE was applied to the rat small intestine in vivo and the recovery of the small intestine was observed during one week post treatment. The electrical parameters used were shown to be strong enough to initially cause complete cellular destruction. The extracellular matrix, however, appeared undamaged and the structure of the small intestine remained intact. The intestine showed signs of recovery, developing an epithelial layer at 3 days post treatment and regenerating mucosa, submucosa, and muscular layers within a week. These results suggest that the small intestine is only temporarily affected by NTIRE, indicating that this procedure can be utilized for abdominal cancer treatment while minimizing collateral damage to adjacent tissues. In addition to examining the recovery of the artery for cancer treatment applications, the potential use of NTIRE to develop a decellularized arterial scaffold was also investigated. The tissue scaffold is a key component for tissue engineering and the extracellular matrix is nature's ideal scaffold material. Two different methods for applying NTIRE to the artery were compared; the results obtained when plate electrodes were applied across the rat carotid artery were compared to the case when endovascular electrodes were applied to the rabbit iliac artery in a minimally invasive fashion. Both methods were shown to preserve the native extracellular matrix and produce a scaffold that is functional and facilitates recellularization. At 3 days post NTIRE, the immune system had decellularized the electroporated tissue, leaving behind a functional scaffold. The endothelial regrowth at 7 days after treatment indicates that the extracellular matrix still maintained its important components to support cell growth. In addition, this endothelial layer shows promise for the tissue scaffold, helping it to avoid issues such as thrombogenicity that many small diameter scaffolds face.

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